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Health-Related Quality of Life and Mortality in a General and Elderly Population of Patients With Type 2 Diabetes (ZODIAC-18)

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OBJECTIVE — Diabetes negatively impacts the health-related quality of life (HRQOL) of patients with type 2 diabetes. An earlier analysis showed HRQOL to be associated with mortality, which suggests that measuring HRQOL could have clinical implications. We studied the association between HRQOL and total and cardiovascular mortality in patients with type 2 diabetes during long-term follow-up and specifically focused on old age and sex differences.

RESEARCH DESIGN AND METHODS — HRQOL was measured in a prospectively followed cohort of 1,353 patients with type 2 diabetes using the RAND-36. Cox proportional hazard models were used to measure the independent effect of baseline HRQOL on mortality.

RESULTS — During a mean follow-up of 9.6 years, 570 (42%) patients died, 280 of whom died of cardiovascular disease (49%). The Physical Component Score (PCS) and the Mental Component Score (MCS) were inversely associated with total mortality, with hazard ratios of 0.988 (95% CI 0.983–0.993) and 0.990 (95% CI 0.985–0.995), respectively. A 10-point-higher score on the PCS and MCS decreased the risk for total mortality by 11 and 10%, respectively. An inverse relationship with mortality was also seen for men, women, and for patients aged >75 years. Mental health was significantly related to mortality in men but not in women.

CONCLUSIONS — Lower physical and mental HRQOL was associated with a higher total mortality and cardiovascular mortality in patients with type 2 diabetes; this is also the case when studying men and women and the elderly separately. The dimension mental health, related to depression and anxiety, was only associated with mortality in men, not in women.

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Diabetes often leads to the development of physical disabilities that, in turn, can have a detrimental effect on a patient's quality of life (QOL) (1). The importance of optimizing health-related QOL (HRQOL) has increasingly been recognized, not only because it represents an important goal for health care on its own but also because of the associations between poor HRQOL and adverse outcomes in people with type 2 diabetes, including poor response to therapy, disease progression, and even mortality (2–6).

The relationship between HRQOL and mortality in patients with diabetes has been investigated previously in three studies (4–6). López Revuelta et al. (4) showed perceived mental health to be an independent predictor of morbidity and mortality in patients with end-stage renal disease. Most of the patients in this study had diabetes (65%). In a recently published study, the EQ-5D questionnaire was used to study the relationship between HRQOL and mortality, and lower HRQOL was associated with a higher mortality rate (5). Our study group previously showed the physical component summary of the RAND-36 to be an independent marker for total mortality in patients with type 2 diabetes (6). The investigators in two of three aforementioned studies reported results for individual health dimensions (4,6). Physical functioning and general health in Kleefstra et al.'s study (6) and general health, mental health, and role limitations due to emotional problems in López Revuelta et al.'s study (4) were associated with total mortality. Although previous studies (7–9) have shown an inverse relationship between HRQOL and mortality in the elderly population, no study has specifically focused on elderly patients with type 2 diabetes. Traditional risk factors become less predictive of mortality at increasing age (10). HRQOL is therefore of interest for elderly patients and may become increasingly important to clinicians for its predictive value.

After these three studies, questions still remain regarding the relationship between the different health dimensions and mortality, the relationship between HRQOL and mortality in elderly patients with type 2 diabetes, and whether the relationship between HRQOL and mortality is different between men and women. The purpose of this study was to revisit the association between HRQOL and mortality after a longer follow-up period (10 years), with a special focus on the elderly (aged >75 years) and on possible sex differences.

RESEARCH DESIGN AND METHODS

In 1998, in the Zwolle region of the Netherlands, a large diabetes project was initiated. In the Zwolle Outpatient Diabetes Project Integrating Available Care (ZODIAC), general practitioners were assisted by hospital-based diabetes specialist nurses in providing care for patients with type 2 diabetes. As part of this project, patients with type 2 diabetes in 32 primary-care practices con-

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sulted (and still consult) these specialist nurses on an annual basis. Patients with a very short life expectancy (including patients with active cancer) and patients with insufficient cognitive abilities were excluded from the study. All patients with type 2 diabetes were identified during the first 2 years of the project. Any patients being treated by an internal medicine specialist (20%) were excluded, as they were no longer in the primary-care setting. Five percent of patients were excluded because of a short life expectancy or because they had insufficient cognitive abilities to complete the necessary questionnaires. A total of 1,353 (90%) patients agreed to participate in the study. The ZODIAC study was approved by the medical ethics committee, and all patients provided informed consent. The details of this study have been published previously (11).

Baseline data, collected in 1998 and 1999, included the RAND-36 questionnaires, a full medical history including the presence or absence of macrovascular complications, the use of medication, and tobacco consumption. Laboratory and physical assessment data were collected annually and included a lipid profile, A1C, serum creatinine, urinary albumin, urinary creatinine, blood pressure, weight, and height. Subsequently, life status and causes of death were retrieved from the records maintained by the hospital and the general practitioners. The causes of death were coded according to theICD-9.

The RAND-36 is considered a generic measure as it is used to assess aspects of health that are relevant to any individual's functional status and well being (12,13). The RAND-36 consists of 36 questions covering nine aspects of health status: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, mental health, and health change. The scores for questions relating to each scale are summed and rescaled to a 100-point scale, where 100 is the best possible score and 0 the worst. The nine scales in the RAND-36 can further be divided into two component summaries: a physical component summary (PCS) and a mental component summary (MCS) (12). Low PCS scores indicate substantial limitations in self-care, physical and social activities, severe bodily pain, or frequent tiredness. Low MCS scores indicate frequent psychological distress and substantial social and role limitations due to emotional problems.

To study mortality, standardized mortality ratios were calculated for total and cardiovascular mortality using general mortality reference rates from the Netherlands (http://statline.cbs.nl/statweb/). Cox proportional hazard modeling was used to assess the association between HRQOL and total mortality and cardiovascular mortality. The health dimensions and component scales all have a different mean value between countries. Comparing scales between countries is difficult; therefore, we transformed the scales. The transformation used is a linear T-score transformation with reference data from the Netherlands (14), which has the advantage of making the different dimensions of health easier to interpret without further reference to normative data (12,15). This results in scores for all the dimensions and the summary scores to have a mean (±SD) of 50 ± 10. The use of the same mean and SD for purposes of transforming scores has the advantage of permitting comparisons of mean scores for HRQOL across countries (16).

A model was constructed that included all possible confounders in the analysis (see below). Separate analyses were performed to study the effect of age and sex on mortality. For the age-specific analysis, patients were stratified into two age-groups, those aged >75 years and those aged ≤75 years. For the sex-specific analysis, we investigated whether significant interaction takes place between sex and HRQOL. Subsequently, we performed multivariate analyses stratified according to sex. The following variables as possible confounders were included (age, sex, smoking [yes/no], duration of diabetes, serum creatinine, BMI, systolic blood pressure, total-to-HDL cholesterol ratio, macrovascular complications [yes/no], use of statins [yes/no], insulin use [yes/no], and urinary albumin-to-creatinine ratio). The proportional hazards assumption was examined using log (−log) survival plots. The parallel lines in the plots indicate that the assumption was met. All tests were two sided, and analyses were performed with SPSS, version 15.0.1 (SPSS, Chicago, IL).

Table 1—*Baseline characteristics*

Characteristics	Total	Deceased patients	Survived patients
n	1,353	570	783
Age (years)	67.8 ± 11.7	75.3 ± 8.6	62.4 ± 10.6†
Female (%)	57.6	57.2	57.9
Diabetes duration (years)	6 (3–11)	7 (3–13)	5 (2–10)†
Smoking (%)	18.6	14.8	21.4
BMI (kg/m²)	28.9 ± 4.8	28.3 ± 4.7	29.4 ± 4.7†
Systolic blood pressure (mmHg)	153 ± 25	156 ± 27	152 ± 24*
A1C (%)	7.5 ± 1.2	7.4 ± 1.3	7.5 ± 1.2
Creatinine clearance (ml/min)	73.9 ± 28.1	60.3 ± 22.2	83.8 ± 27.9†
Total-to-HDL ratio	5.2 ± 1.6	5.1 ± 1.6	5.2 ± 1.5
Albumin-to-creatinine ratio	2.1 (1.0–7.2)	3.9 (1.4–12.3)	1.6 (0.9–4.4)†
Macrovascular complications (%)	32.7	46.1	23.0†
Age >75 years (%)	27.6	53.3	8.9†
PCS score	71.6 (48.7–86.7)	61.3 (41.5–80.5)	76.8 (55.8–89.2)†
MCS score	76.8 (59.3–87.6)	71.3 (52.3–84.1)	79.8 (61.8–88.8)†

Data are means ± SD for normally distributed data, median (interquartile range) for nonnormally distributed data, or percent. *$P < 0.05$; †$P < 0.001$.

RESULTS — Patient characteristics at baseline are presented in Table 1. After a median follow-up period of 9.6 years, 570 of 1,353 patients had died (42%). Life status was not known for 20 patients (1%), and causes of death were unknown for 29 patients (5%); 238 deaths (42%) had cardiovascular causes and 122 deaths (21%) were due to cancer. HRQOL data were available and complete for 1,053 patients (78%). The standardized mortality ratios (95% CIs) for total mortality and cardiovascular mortality were 2.35 (95% CI 1.77–3.04) and 2.67 (2.36–3.05).

The hazard ratios (HRs) for total mortality for the PCS and MCS were 0.988 (95% CI 0.983–0.993) and 0.990 (0.985–0.995), respectively. A one-point-higher score on the PCS and MCS decreases the risk for mortality by 1.2 and 1.0%, respectively. This means that a clin-

Table 2—*Relationship between HRQOL and total and cardiovascular mortality*

RAND-36 dimensions 1-point higher score	HR (95%CI)* Total mortality	HR (95%CI)* Cardiovascular mortality
PCS	**0.988 (0.983–0.993)**	**0.988 (0.977–0.999)**
MCS	**0.990 (0.985–0.995)**	**0.987 (0.975–0.999)**
Physical functioning	**0.988 (0.984–0.991)**	**0.988 (0.979–0.997)**
Social functioning	**0.992 (0.988–0.996)**	0.996 (0.986–1.006)
Role functioning, physical	**0.996 (0.993–0.999)**	**0.995 (0.991–0.999)**
Role functioning, emotional	**0.997 (0.994–0.999)**	**0.994 (0.988–0.999)**
Mental health	**0.993 (0.989–0.998)**	**0.987 (0.976–0.998)**
Bodily pain	**0.994 (0.991–0.998)**	0.998 (0.989–1.008)
Vitality	**0.993 (0.989–0.998)**	0.995 (0.984–1.006)
General health perception	**0.984 (0.978–0.991)**	**0.979 (0.962–0.995)**
Health change	0.997 (0.992–1.003)	1.008 (0.994–1.022)

*Corrected for age, sex, smoking, duration of diabetes, serum creatinine, BMI, systolic blood pressure, total-to-HDL cholesterol ratio, macrovascular complications, use of statins, insulin use, and urinary albumin-to-creatinine ratio. Significant relationships are indicated in bold.

ically meaningful increase of a 10-point-higher score, on a 100-point scale, on the PCS and MCS, decreased the risk for mortality by 11% (0.988 to the power 10) and 10%, respectively.

For cardiovascular mortality, the HRs of PCS and MCS were 0.988 (95% CI 0.977–0.999) and 0.987 (0.975–0.999), respectively. Eight of nine health dimensions were related to total mortality, and five health dimensions were associated with cardiovascular mortality (Table 2).

Elderly patients

PCS and MCS were also inversely associated with mortality in the subgroup of elderly patients (aged >75 years) with HRs of 0.989 (95% CI 0.981–0.996) and 0.991 (0.984–0.999), respectively (Table 3). For the subgroup of younger patients (aged ≤75 years), HRs for PCS and MCS were 0.987 (0.980–0.993) and 0.988 (0.981–0.995), respectively. In the subgroup of elderly patients, three of nine health dimensions were inversely associated with total mortality with lowest HRs for physical functioning and general health perception.

Sex-related differences

We found a significant interaction between mental health and sex ($P = 0.042$) (Table 4). After adding the interaction term between sex and mental health to the model, the association between mental health and total mortality became more pronounced (HR 0.976 [95% CI 0.960–0.994]). The PCS and MCS were inversely associated with total mortality for both women and men. For female patients, the HRs were 0.988 (0.982–0.994) and 0.992 (0.985–0.998) for PCS and MCS, respectively. For male patients, the HRs for PCS and MCS were 0.988 (0.981–0.996) and 0.987 (0.979–0.995).

A total of six of nine health dimensions were related to total mortality for women and five of nine for men. There were three differences: the health dimension role functioning (physical) was significantly related to mortality in women but not in men, and bodily pain was significantly related to women but not in men, although absolute HRs did not really differ. Mental health was significantly related to mortality in men but not in women, with notable differences also in HR (0.984 [95% CI 0.976–0.992]) vs. 0.998 (0.992–1.004). When looking at the individual five questions from which the mental health dimension is composed, all five relating to depression and anxiety, these five questions were related to mortality in men but none in women (data not shown).

Analyzing of the model with the variable "incomplete questionnaire" (instead of the RAND-36 scores), patients who did not complete the RAND-36 had an increased total mortality risk compared with patients who completed the questionnaire. When excluding the first 2 years of follow-up, the relationship between the two component summaries and total and cardiovascular mortality was still present and did not relevantly change (data not shown). Survival was also predicted by the factors age, sex, serum creatinine, and albumin-to-creatinine ratio. The proportional hazard assumptions were met for all analyses.

CONCLUSIONS

— After a median follow-up period of almost 10 years, total and cardiovascular mortality was increased for type 2 diabetic patients who had a lower HRQOL at baseline. Both the PCS and MCS were related to total and cardiovascular mortality regardless of confounders such as age and sex. A 10-point-higher score, on a 100-point scale, on the PCS and MCS decreased the risk for mortality by 11 and 10%, respectively. These effects appear to be clinically relevant and comparable with a 1% decrease in A1C (17). Our study supports the recommendations to include measurement and integration of health status in clinical practice (18,19). As it is difficult to interpret the applicability of our results into

Table 3—*Relationship between HRQOL and total mortality stratified according to age*

RAND-36 dimensions 1-point higher score	HR (95%CI)* Total mortality (aged >75 years)	HR (95%CI)* Total mortality (aged ≤75 years)
PCS	**0.989 (0.981–0.996)**	**0.987 (0.980–0.993)**
MCS	**0.991 (0.984–0.999)**	**0.988 (0.981–0.995)**
Physical functioning	**0.985 (0.979–0.992)**	**0.988 (0.983–0.993)**
Social functioning	**0.992 (0.987–0.997)**	**0.990 (0.985–0.996)**
Role functioning, physical	0.997 (0.993–1.000)	**0.994 (0.991–0.998)**
Role functioning, emotional	0.998 (0.994–1.001)	**0.996 (0.992–0.999)**
Mental health	0.995 (0.988–1.003)	**0.992 (0.985–0.999)**
Bodily pain	0.995 (0.989–1.000)	**0.993 (0.988–0.998)**
Vitality	0.996 (0.989–1.003)	**0.992 (0.986–0.998)**
General health perception	**0.983 (0.973–0.994)**	**0.984 (0.975–0.993)**
Health change	0.997 (0.987–1.006)	0.999 (0.991–1.006)

*Corrected for age, sex, smoking, duration of diabetes, serum creatinine, BMI, systolic blood pressure, total-to-HDL cholesterol ratio, macrovascular complications, use of statins, insulin use, and urinary albumin-to-creatinine ratio. Significant relationships are indicated in bold.

Table 4—*Relationship between HRQOL and total mortality stratified according to sex*

RAND-36 dimensions 1-point higher score	HR (95%CI)* Male subjects	HR (95%CI)* Female subjects
PCS	**0.988 (0.981–0.996)**	**0.988 (0.982–0.994)**
MCS	**0.987 (0.979–0.995)**	**0.992 (0.985–0.998)**
Physical functioning	**0.988 (0.983–0.994)**	**0.988 (0.982–0.993)**
Social functioning	**0.990 (0.984–0.996)**	**0.993 (0.988–0.998)**
Role functioning, physical	0.997 (0.993–1.001)	**0.996 (0.993–0.999)**
Role functioning, emotional	0.996 (0.992–1.001)	0.997 (0.994–1.000)
Mental health	**0.984 (0.976–0.992)**	0.998 (0.992–1.004)
Bodily pain	0.994 (0.989–1.000)	**0.994 (0.989–0.999)**
Vitality	**0.993 (0.987–0.999)**	**0.993 (0.988–0.999)**
General health perception	**0.986 (0.976–0.996)**	**0.983 (0.974–0.992)**
Health change	0.998 (0.989–1.006)	0.997 (0.989–1.004)

*Corrected for age, smoking, duration of diabetes, serum creatinine, BMI, systolic blood pressure, total-to-HDL cholesterol ratio, macrovascular complications, use of statins, insulin use, and urinary albumin-to-creatinine ratio. Significant relationships are indicated in bold.

daily practice, we present an example: if a female patient has a score of 40 on the PCS, this means that her absolute score is 10 points lower than the mean (using the T-score transformation, the PCS has a mean of 50). Her HR for mortality would be 11.4% higher (0.988 to the power of 10).

In our previous study, which had a median follow-up period of 5.8 years, the only significant association we found was between the PCS score and total mortality, and two separate health dimensions: 'physical functioning' and 'general health perception' (6). The association between the MCS score and mortality was 1.008 (CI 0.994–1.022). In our present study, with almost 10 years of follow-up, the relationship is quite different, and MCS is now inversely associated with mortality. This may imply that low MCS scores can only predict mortality after a longer follow-up period. Furthermore, the relationships between the separate health dimensions and mortality have become more pronounced, with most dimensions being inversely related to mortality.

For the sex-specific analysis, an interesting interaction between mental health and sex existed. Such an interaction could mean that sex has an effect on the relationship between mental health and mortality. Stratification for sex revealed one relevant difference: mental health was related to mortality in men only. A 10-point-higher score on the dimension mental health decreased mortality risk with 15% in men. At baseline, women rated their mental health worse than men, with a median score of 79 vs. 71 in men ($P = 0.001$). Patients with decreased scores on the mental health dimension have symptoms related to depression and anxiety (20). This difference between men and women in our cohort could imply that poorer mental health, although less prevalent in man compared with women, has a greater effect on mortality in men. The individual questions from which the mental health dimension is composed are related to depression and anxiety, and there is some evidence in a nondiabetic population that depression effects mortality risk in men more than in women (21).

In the age-specific analysis, in which we stratified for age, many associations were not significant for patients aged >75 years. However, these differences do not seem to be clinically relevant and are probably caused by the reduction in sample size after stratification. According to the various subgroup analyses, the health dimensions physical functioning, social functioning, and general health were the most consistent predictors for mortality. Previous studies (22,23) have shown that a patient's self-rated health status is consistently associated with mortality.

Due to this study's observational design, it is not clear whether there is a true causal relationship between HRQOL and mortality. The question remains whether HRQOL is a modifiable risk factor or just a marker of disease burden. No randomized controlled trials have been performed in which an attempt was made to specifically improve HRQOL specifically. Whether HRQOL is a causal factor for mortality, we first would need to identify a possible treatment strategy to improve HRQOL. A recent meta-analysis could not identify psychosocial interventions with clinically relevant benefit with regard to physical and mental health in patients with diabetes (24). Developing such strategies remains an important challenge and could have implications for the understanding of interaction between physical and mental health. Patients with diabetes are also more prone to depression compared with patients without diabetes (25). The dimension mental health is correlated to depression (13), and depression is independently associated with a lower HRQOL and mortality (25); hence, one could hypothesize that treating depression, and indirectly HRQOL, may increase survival. Such a hypothesis needs to be investigated, however. Several trials have been performed in depressed patients following a myocardial infarction, but all interventions applied did not increase survival (26).

There are additional limitations to our study. Twenty-two percent of our patient population did not complete the RAND-36 questionnaire. As not completing the questionnaire was associated with an increased mortality, it is likely that the relationships between the HRQOL indexes and (cardiovascular) mortality are underestimated in this study. There may also be additional confounders, such as depression and social economic status, which we did not take into account and which may, therefore, have influenced the outcome (25). Furthermore, no adjustments were made for a history of diseases other than cardiovascular disease. However, after excluding the first 2 years of follow-up from the analysis, the relationship between HRQOL and (cardiovascular) mortality remained largely unchanged. Excluding the first 2 years of follow-up could correct for severe comorbidity or undiagnosed cancer at the start of the study, which could have influenced outcome.

Specific strengths of our study include the prospective nature of the design and a follow-up period of almost 10 years. The number of deaths after the 10-year period was sufficient to allow reliable estimates of associations with mortality. We also performed a T-score transformation, which has the advantage of permitting comparisons of mean scores for health in different countries (15).

Our study shows that a decrease in HRQOL is associated with an increase in (cardiovascular) mortality among young as well as elderly type 2 diabetic patients. HRQOL instruments may become an increasingly useful clinical tool to not only identify those patients with a low HRQOL but also to identify those patients with an associated increase in mortality risk. This study supports the clinical predictive use of HRQOL measures in combination with the well established risk factors for the assessment of mortality risk for patients type 2 diabetes.

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G.W.D.L. researched data, contributed to the discussion, and wrote the manuscript. K.J.J.V.H. researched data, contributed to the discussion, and wrote the manuscript. N.K. researched data, contributed to the discussion, and edited the manuscript. K.H.G. researched data, contributed to the discussion, and edited the manuscript. R.O.B.G. contributed to the discussion and edited the manuscript. H.J.G.B. researched data, contributed to the discussion, and edited the manuscript.

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References

1. Gregg E, Beckles G, Williamson D, Leveille S, Langlois J, Engelgau M, Narayan KM. Diabetes and physical disability among older U.S. adults. Diabetes Care 2000;23:1272–1277
2. Jacobson AM, de Groot M, Samson JA. The evaluation of two measures of quality of life in patients with type 1 and type 2 diabetes. Diabetes Care 1994;17:267–274
3. G'afvels C, Lithner F, Börjeson B. Living with diabetes: relationship to gender, duration and complications: a survey in northern Sweden. Diabet Med 1993;10: 768–773
4. López Revuelta K, Garcia Lopez FJ, de Alvaro Moreno F, Alonse J, the CALVIDIA Group. Perceived mental health at the start of dialysis as a predictor of morbidity and mortality in patients with end-stage renal disease (CALVIDIA study). Nephrol Dial Transplant 2004;19:2347–2353
5. McEwen LN, Kim C, Haan MN, Ghosh D, Lantz PM, Thompson TJ, Herman WH. Are health related quality of life and self rated health associated with mortality? Insight from Translating Research Into Action for Diabetes (TRIAD). Prim Care Diab 2009;3:37–42
6. Kleefstra N, Landman GW, Houweling ST, Ubink-Veltmaat LJ, Logtenberg SJ, Meyboom-de Jong B, Coyne JC, Groenier KH, Bilo HJ. Prediction of mortality in Type 2 diabetes from health related quality of life (ZODIAC-4). Diabetes Care 2008;31:932–933
7. Tibblin G, Svardsudd K, Welin L, Erikson H, Larsson B. Quality of life as an outcome variable and a risk factor for total mortality and cardiovascular disease: a study of men born in 1913. J Hypertens 1993;11: S81–S86
8. Dominick KL, Ahern FM, Gold CH, Heller DA. Relationship of health-related quality of life to healthcare utilization and mortality among older adults. Aging Clin Exp Res 2002;14:499–508
9. Tsay SU, Chi LY, Lee CH, Chou P. Health-related quality of life as a predictor of mortality among community dwelling older persons. Eur J Epidemiol 2007;22: 19–26
10. De Ruijter W, Westendorp RG, Assendelft WJ, Den Elzen WPJ, De Craen AJ, Le Cessie S, Gussekloo J. Use of Framingham risk score and new biomarkers to predict cardiovascular mortality in older people: population based observational cohort study. BMJ 2009;338:a3083
11. Ubink-Veltmaat LJ, Bilo HJ, Groenier KH, Rischen RO, Meyboom-de Jong B. Shared care with task delegation to nurses for type 2 diabetes, a prospective observational study. Neth J Med 2005;63:103–110
12. Ware JE, Kosinski M, Keller SD. SF-36 *Physical and Mental Health Summary Scales: A Users Manual*. Boston, The Health Institute, 1994
13. van der Zee KI, Sanderman R, Heyink J. [The psychometric properties of the SF-36-item Short Form Health Survey in a Dutch population.] Tijdschrift voor Sociale Gezondheidszorg 1994;4:183–191
14. Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R, Sprangers MA, te Velde A, Verrips E. Translation, Validation, and Norming of the Dutch Language Version of th SF-36 Health Survey in Community and Chronic Disease Populations. J Clin Epidemiol 1998;51:1055–1068
15. Ware JE, Kosinski M, Bayliss MS, McHorney CA, Rogers WH, Raczek AE. Comparison of methods for scoring and statistical analysis of SF-36 health profiles and summary measures: Summary of results from the Medical Outcomes Study. Med Care 1995;33(Suppl. 4):AS264– AS279
16. Ware JE, Gandek B, Kosinski M, Aaronson NK, Apolone G, Brazier J, Bullinger M, Kaasa S, Leplège A, Prieto L, Sullivan M, Thunedborg K. The Equivalence of SF-36 Summary Health Scores Estimated Using Standard and Country-Specific Algorithms in 10 Countries: Results from the IQOLA Project. J Clin Epidemiol 1998;51:1167–1170
17. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405–412
18. Glasgow RE, Peeples M, Skovlund SE. Where is the patient in diabetes performance measures? The case for including patient-centered and self-management measures. Diabetes Care 2008;31:1046–1050
19. Spertus JA. Evolving applications for patient-centered health status measures. Circulation 2008;11:118;2103–2110
20. Ali S, Stone M, Skinner TC, Robertson N, Davies M, Khunti K. The association between depression and health-related quality of life in people with type 2 diabetes: a systematic literature review. Diabete Metab Res Rev 2010;26:75–89
21. Ferketich AK, Schwartzbaum JA, Frid DJ, Moeschberger ML. Depression as an antecedent to heart disease among women and men in the NHANES I study. National Health and Nutrition Examination Survey. Arch Intern Med 2000;160:1261–1268
22. Idler EL, Benyamini Y. Self-rated health and mortality: a review of twenty-seven community studies. J health Soc Behav 1997;38:21–37
23. Rakowski W, Fleishman JA, Mor V, Bryant SA. Selff-assesment of health and mortality among elder persons. Do questions other than global self-rated health predict mortality? Res Aging 1993;15:92–116
24. Harkness E, Macdonald W, Valderas J, Coventry P, Gask L, Bower P. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. Diabetes Care 2010; 33:926–930
25. Katon WJ, Rutter C, Simon G, Lin EH, Ludman E, Ciechanowski P, Kinder L, Young B, Von Korff M. The association of co-morbid depression with mortality in patients with type 2 diabetes. Diabetes Care 2005;28:2668–2672
26. Carney RM, Freedland KE. Does treating depression improve survival after acute coronary syndrome? Br J Psych 2007;190: 467–468